REMARKS

Applicant wishes to thank Examiner Li for taking the time to speak with Applicant's representative on July 3, 2008, regarding product claims 41 and 44. In view of the discussion, Applicant respectfully requests entry of amendments to claims 1, 11, 25, and 45. Please cancel claims 2, 15, 18-24, 26, 41-44, and 47-52, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including paragraphs [0111], [0053], [0090], [0121], and [0123], and Figures 2, 5, 10, and 11, and the originally filed claims and, therefore, do not add new matter.

Applicant submits that pending claims 1, 3-14, 16, 17, 25, 27-40, 45, and 46 are in condition for allowance, or are in better condition for presentation on appeal, and respectfully requests that the claims as amended be entered.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1, 3-14, 16-19, 21-25, 27-41, and 43-52 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. As claims 18, 19, 21-24, 41, 43, 44, and 47-52 have been canceled, the rejection as applied to these claims is rendered moot.

Applicant traverses the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Regarding step a of claims 1, 25, and 45, the Office Action alleges, in pertinent part, that it is unclear what the chimeric DNA constructs contain beyond one of the 5' or 3' regulatory sequences. Applicant submits that as stated in Miles Laboratories, Inc. v. Shandon Inc., 27 U.S.P.Q.2d 1123 (Fed. Cir. 1993), cert denied, 510 U.S. 1100 (1994):

> "The test for definiteness is whether one skilled in the art would have understood the bounds of the claim when read in light of the specification . . .. If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, 112 demands no more . . .."

Respectfully, Applicant submits that the specification clearly apprises one of skill in the art the scope of the invention. For example, at paragraph [0089] the specification recites:

> "Figure 1A shows the PCR procedure used to generate recombinant DNA between mouse and human sequences. Two BACs carrying either mouse (BAC-1) or the human orthologue of the mouse gene (BAC-2) gene are created. The BACs may include the control region contiguous to the coding region. Two PCR products (pA and pB) are made, both are hybrid products between human and mouse DNA. The first half of pA is 2 kb upstream of mouse DNA from the beginning of the coding region and the second half is 2 kb human DNA starting at the first codon ATG of the human coding region. Likewise, the half of pB is 2 kb human DNA containing the last codon TAG at the junction of the second half that is 2 kb downstream of mouse DNA from the TAG."

Clearly, the skilled artisan would understand from this example that pA and pB represent the chimeric constructs recited in the claims. Further, the skilled artisan would understand from this example that, in addition to comprising 3' and 5' regulatory sequences (e.g., start and stop codons), the chimeric constructs comprise non-coding sequences of a mouse or non-human animal gene and sequences encoding the human orthologue.

In another example, at paragraph [0092], the specification recites:

> "A second round of PCR can be used to generate PCR products having DNA from both mouse and human. Figure 1C, for example, shows the use of PCR primers to generate fragments labeled Product 5 and Product 6, that have a junction between the human and mouse DNA at the ends of the coding region of the gene. As shown in Figure 1C, there is an overlapping 20 bases between 3' end of Product 1 and 5' end of Product 2. Using primers p1 and p4, and the two product[sic], PCR- 5 generate ~4kb product 5 that is a fused DNA at the overlapping region. Likewise, ~4 kb Product 6 is generated as a fused DNA between Products 3 and 4."

As in the previous example, one of skill in the art would clearly appreciate that Product 5 and Product 6 represent the chimeric constructs recited in the claims. Again, the skilled artisan would understand from this example that the chimeric constructs comprise non-coding sequences

of a mouse or non-human animal gene and sequences encoding the human orthologue. Further, at paragraph [0111], the specification recites:

> "As outlined in Figures 9 to 11, the construction of a pair of head and tail chimeras, and subsequent fusion product has been completed. The head chimera is derived from 1,169 bp upstream region of the first codon GTG of mouse PXR and from 1,929 bp downstream region of the first codon GTG of human PXR. This chimera has been made by a two-step PCR procedure . . . the first PCR generated 1,169 bp and 1,929 bp products from corresponding regions, and the second PCR has generated the chimeric product via 40 bp overlapping segment between the two initial products. The resultant product is called 5' head chimera. Likewise, 3' tail chimera has been constructed by the fusion of 1,194 bp human and 1,223 bp mouse segments (Figure 9). The last terminator codon is at the junction of two segments as illustrated in Figure 9."

Clearly, the skilled artisan would understand from this example that 5' head chimera and 3' tail chimera represent the chimeric constructs recited in the claims. Further, the skilled artisan would also understand from this example that in addition to comprising 3' and 5' regulatory sequences (e.g., start and stop codons), the chimeric constructs comprise non-coding sequences of a mouse gene (PXR) and sequences encoding the human orthologue (PXR).

As such one of skill in the art reading the claims in light of the specification would understand that, in addition to comprising regulatory regions, the chimeric constructs as claimed would also contain sequences comprising non-coding sequences of a mouse or non-human animal gene and sequences encoding the human orthologue of the mouse or non-human animal gene. Therefore, in view of the test for definiteness recited in Miles Laboratories, nothing more is required.

Regarding step b of claims 1, 25, and 45, the Office Action alleges that "the ends of the human DNA do not comprise the at least two chimeric DNA constructs in the context of the claims, and further that it is unclear where the ends ligate to (e.g., together), and whether it's between any random chimeric DNA constructs, such as two chimeric constructs both contain a 5'-regulatory sequence." While not acquiescing to the reasoning offered in the Office Action, in

order to expedite prosecution toward allowance, the claims have been amended to recite "ligating the human DNA ends of the first and second chimeric DNA constructs." Since "ligation," by definition, means to join molecules or molecular fragments together with a bond,[1] the skilled artisan would understand the metes and bounds of the claims.

Regarding step c, the Office Action alleges that because the ligated constructs comprises human sequences flanked by mouse sequences, it is unclear how the human sequence in the third construct differs from that of the ligated chimeric DNA construct before it recombines with second construct. While not acquiescing to the reasoning offered in the Office Action, in order to expedite prosecution toward allowance, the claims have been amended to recite "thereby allowing for modification of human DNA of the ligated chimeric DNA constructs." The ligating step makes regions within the human sequence available for modification (e.g., insertion of restrictions sites, positive selection markers, and/or negative selection markers). For example, at paragraph [0112], the specification recites that 5' head and 3' tail chimera were merged to create a Cla I site (see also, Figure 10), followed by insertion of a tetA gene into the Cla I site (Figure 11). Further, as shown in Figures 2 and 6, the chimeras allow for insertion of positive and/or negative selection markers resulting in Product 7 (i.e., a ligated construct generated from two chimeras), which may be recombined to form Product 8 (i.e., third DNA construct; see, e.g., Figure 3). Again, as the test for definiteness is whether one skilled in the art would have understood the bounds of the claim when read in light of the specification, Applicant submits that one of skill in the art would understand the difference between the human sequence in the third construct and the ligated chimeric DNA construct.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

---

[1] See, e.g., Oxford Dictionary of Biochemistry and Molecular Biology, Revised Ed., 2001, Oxford University Press, Inc., New York, NY.

Rejections Under 35 U.S.C. §102

Claim 41 stands rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Shiao et al. as evidenced by Wikipedia Receptor, 2008. As claim 41 has been canceled, the rejection as applied to this claim is rendered moot.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Claim 41 stands rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Divoky et al. as evidenced by Wikipedia Receptor, 2008. As claim 41 has been canceled, the rejection as applied to this claim is rendered moot.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Rejections Under 35 U.S.C. §103

Claims 18, 19, 21-24, and 47-52 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Divoky et al. in view of Heintz et al. As claims 18, 19, 21-24, and 47-52 have been canceled, the rejection as applied to these claims is rendered moot.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Claims 41 and 44 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Divoky et al. in view of Xie et al. As claims 41 and 44 have been canceled, the rejection as applied to these claims is rendered moot.

For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Conclusion

Applicant submits that pending claims 1, 3-14, 16, 17, 25, 27-40, 45, and 46 are in condition for allowance, or are in better condition for appeal. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this submission.

Please charge Deposit Account 07-1896 in the amount of $230.00 for a Two Month Extension of Time. The Commissioner is hereby authorized to charge any additional fees required by this submission, or make any credits or overpayments, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

Date: July 25, 2008

Daryl A. Basham, J.D., Ph.D.
Registration No. 45,869
Telephone: (858) 677-1429
Facsimile: (858) 677-1465

DLA Piper US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213